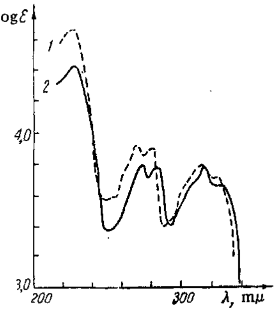
THE STRUCTURE OF BUCHARIDINE

Z. Sh. Faizutdinova, I. A. Bessonova, Ya. V. Rashkes, and S. Yu. Yunusov

Khimiya Prirodnykh Soedinenni, Vol. 6, No. 2, pp. 239–243, 1970
UDC 547.944/945

In separating the total alkaloids of Haplophyllum bucharicum Litv. and H. foliosum Vved., we isolated a phenolic base with the composition of $C_{19}H_{25}O_4N$, which we called "bucharidine" [1].

Bucharidine has no methoxyl, methylenedioxy, or N-methyl groups. Its IR spectrum has absorption bands at 3470 cm^{-1} (OH) and 1645 cm^{-1} (NH–CO). The UV spectrum of the base (figure) is characteristic for 2, 4-dihydroxyquinoline derivatives. The presence in the NMR spectrum of the alkaloid of a one-proton quartet at τ 2.21 ppm (H_5) and of a three-proton multiplet at τ 2.78 ($H_{6,7,8}$) shows that the benzene ring of the carbostyryl nucleus does not contain substituents. The shift of the signal from H_5 in the weak-field direction by 66 Hz [2] relative to the center of the multiplet of the other aromatic protons, and also the solubility of the alkaloid in alkali shows that the base has a 4-hydroxyquinolin-2-one skeleton.



UV spectra of 2, 4-dihydroxyquinoline (1) and of bucharidine (2).

The absence of a signal from a proton at C_3 shows that the $C_{10}H_{19}O_2$ residue of the molecule is attached to the 4-hydroxyquinolin-2-one nucleus in position 3.

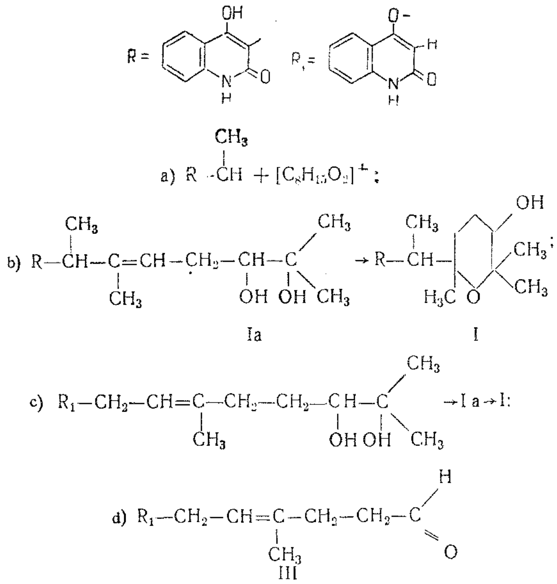
The oxidation of bucharidine by the Kuhn-Roth method led to the formation of acetone; the mass spectrum of the alkaloid has the peak of the M – 59 ion (15% of the main peak), and therefore the side chain contains the element $-O-C(CH_3)_2$. The NMR spectrum of bucharidine showed the following three groups of signals from protons of the side chain: a two-proton multiplet between τ 5.9 and 6.3 $\left(\mathrm{R{-}\overset{|}{C}\underline{H}{-}CH_3}\ \text{and}\ \mathrm{{-}C\underline{H}{-}O{-}}\right)$, a four-proton multiplet at τ 7.7–8.3 $(-O-C-CH_2-CH_2-C-O-)$, a six-proton singlet at τ 8.84, a three-proton doublet at τ 8.77, and a three-proton singlet at τ 8.70 $(C\underline{H}_3-C-C\underline{H}_3,\ C\underline{H}_3-CH,\ C\underline{H}_3-C-)$.

In the mass spectrum of the base, the peak of the molecular ion (m/e 331) has a low intensity. The peak of an ion with m/e 143 is the maximum peak in the spectrum; ions with masses of 188 and 189 are also among the main ones. These facts show that under electron impact the bucharidine molecule decomposes into two parts in such a way that two carbon atoms remain attached to the nucleus (Scheme 1a).

When the alkaloid was deuterated the peak of the molecular ion shifted by three units, and the peak of the ion with m/e 143 by one unit. These facts show that in the bucharidine molecule one active hydrogen is located in the m/e 143 fragment and two others in the element with a mass of 188.

The side chain of the substance consists of ten carbon atoms. It is possible that they form a system of two isoprene units, which is frequently encountered in natural compounds [3].

Considering what has been said above and also the fact that bucharidine is not hydrogenated over a platinum catalyst, has no signals of olefinic protons in the NMR spectrum, and contains three active hydrogens, we have assumed that the double bond of one isoprene unit and the hydroxyl group of the other have joined up to form a cyclic isomer (Scheme 1b).



Scheme 1.

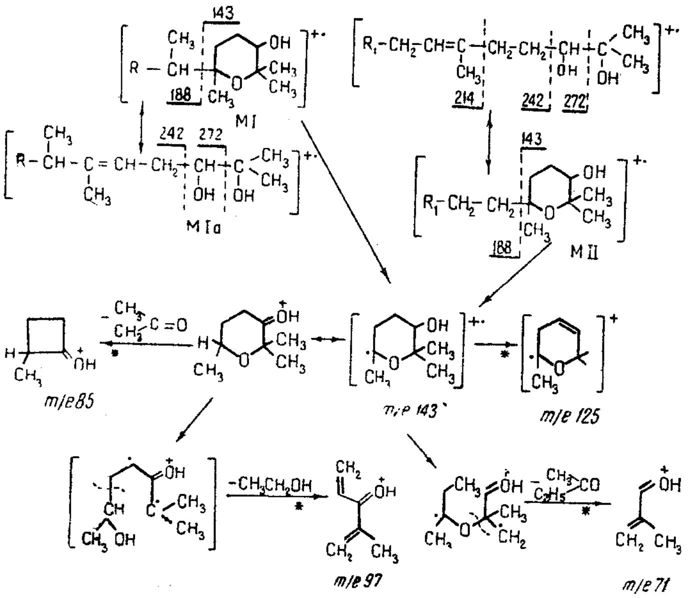
We have given the position of the alcoholic hydroxyl group in bucharidine on the basis of the following considerations. Under the conditions of mass spectrometry, the bucharidine molecule can exist both in the cyclic (I), and in the chain (Ia) forms. The presence in the spectrum of an ion with m/e 242 (M – 89) shows that together with the detachment of a hydroxyisopropyl group from the molecular ion of Ia the splitting out of a fragment 30 amu. (CH—OH) heavier takes place. This is possible only if the hydroxyl group of the side chain occupies the position shown in Formula I.

The composition and UV spectrum of bucharidine are similar to those of bucharaine II, isolated from H. bucharicum [4]. The mass spectra of the two substances differ only slightly. In contrast to bucharidine, which has four C-methyl groups, the NMR spectrum of bucharaine has signals from three C-methyl groups, the signal of one of them being shifted in the weak-field direction. The presence in the NMR spectrum of II of a one-proton singlet from the proton at C_3 and the splitting off of the side chain when this alkaloid is hydrogenated gives grounds for assuming that II is an O-allyl ether from which I can be obtained by a Claisen rearrangement. In actual fact, when this reaction was performed a substance identical with bucharidine was obtained. In bucharaine the γ-carbon atom bears a substituent, and therefore an abnormal Claisen rearrangement [5] takes place (Scheme 1c).

The establishment of the chemical similarity of I and III enabled the position of the alcoholic hydroxyl group in bucharidine to be determined chemically. For this purpose bucharaine was subjected to periodate oxidation, giving an aldehyde III with a mass 60 units smaller than the mass of the initial compound (mol wt 271, mass spectrometry) (Scheme 1d).

Thus, it has been shown that the hydroxyl groups of bucharaine are present on neighboring carbon atoms. This has confirmed the correctness of formula I proposed for bucharidine.

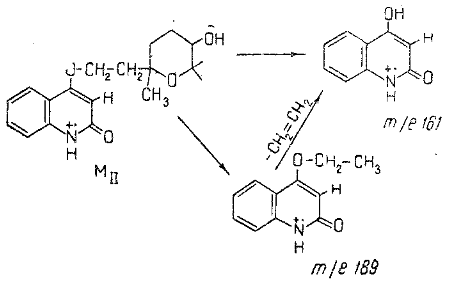
The great similarity of the mass spectra of I and II can be explained by the assumption that those substances can exist both in cyclic and chain forms under the action of electron bombardment while in I there is a shift in the direction of the chain form. Consequently the intensities of the ions produced from the cyclic form are higher in I, and those from the chain form in II (Scheme 2). The formation of an ion with m/e 214 in Ia apparently precedes the migration of the double bond into the conjugated position.



Scheme 2. Fragmentation of bucharidine I and bucharaine II (the symbol* denotes transitions confirmed by metastable peaks).

Ions of the cyclic form	*m/e*	125	97	85	71
	I	29	5	19	30
Relative intensity, %	II	21	3,5	16	25
Ions of the chain form	*m/e*	272	242	214	—
	I	15	1,5	6	—
Relative intensity, %	II	19	4	18	—

The ions with m/e 188 and 189 have different structures in the two bases, the latter ion contains a 4-ethoxy group in the case of substance II and a 4-hydroxy-3-ethyl group in substance I. The formation of a phenolic fragment with m/e 161 (10%) in the degradation of bucharaine and the absence of this peak from the spectrum of I confirms the nature of the differences between I and II.



The alkaloids ravenine and ravenoline have been isolated from the plant Ravenia spectabilis [6]. As in our case, the second alkaloid is a product of the abnormal Claisen rearrangement of the first. However, in contrast to the bucharaine–bucharidine pair, ravenine and ravenoline each contain a single isoprene unit in the side chain.

EXPERIMENTAL

Isolation of bucharidine. The total alkaloids remaining after the separation of bucharaine were separated into a phenolic and a nonphenolic fraction. The phenolic fraction (35 g) was chromatographed on alumina (700 g). Bucharidine was isolated from the ethereal-chloroformic eluates.

Bucharidine (I). The substance obtained had mp 251–252° C (acetone).

Found, %: C 68.5, 68.4; H 7.59, 7.64; N 4.35, 4.26. Mol wt 331 (mass spectrometry). Calculated for $C_{19}H_{25}O_4N$, %: C 68.9; H 7.6; N 4.23. Mol wt 331.398.

Oxidation of bucharidine. A mixture of 0.1 g of bucharidine, 1 g of chromic anhydride, 1 ml of conc H_2SO_4, and 4 ml of water was heated. The volatile products were trapped in a 1% solution of 2, 4-dinitrophenylhydrazine hydrochloride. A precipitate of acetone 2, 4-dinitrophenylhydrazone with mp 123–124° C (ethanol) was formed.

Conversion of bucharaine into bucharidine. A solution of 0.25 g of bucharaine in 5 ml of tetralin was boiled under reflux for 8 hr. Chromatography of the reaction products on alumina gave 0.15 g of a crystalline substance with mp 250–251° C (acetone, methanol). A mixture with bucharidine gave no depression of the melting point, and the IR and mass spectra of the substances compared were identical.

Oxidation of bucharaine. An aqueous solution of 0.15 g of potassium periodate was added to a solution of 0.1 g of bucharaine in 5 ml of methanol. After a day, the precipitate of bucharainal that had deposited was separated off and recrystallized from aqueous methanol, mp 121–122° C.

Bucharainal oxime. Hot solutions of 0.04 g of bucharainal in ethanol and 0.02 g of hydroxylamine hydrochloride in water were mixed, and then a solution of 0.01 g of sodium carbonate was added to the hot mixture. On standing, crystals of bucharainal oxime deposited with mp 181–182° C (ethanol).

Bucharainal 2, 4-dinitrophenylhydrazone. The substance was formed when an ethanolic solution of bucharainal and a 0.1% solution of 2, 4-dinitrophenylhydrazine hydrochloride were mixed; mp 202–203° C (ethanol).

The mass spectra were recorded on a MKh 1303 mass spectrometer fitted with a system for the direct introduction of substances into the ion source, at ~ 100° C with an ionizing voltage of 40 V.

Deuteration was carried out by heating the substances at 100° C in CD_3OD in a sealed tube for a day.

The NMR spectrum was recorded by M. R. Yagudaev on a JNM-4H-100/100 MHz instrument in deuterochloroform with HMDS as internal standard.

CONCLUSIONS

1. A new phenolic base, bucharidine, has been isolated from the mother liquors of Haplophyllum bucharicum.

2. Bucharidine is a 3-substituted derivative of 4-hydroxyquinolin-2-one.

3. Bucharaine has been converted into bucharidine by a Claisen rearrangement.

REFERENCES

1. Z. Sh. Faizutdinova, I. A. Bessonova, and S. Yu. Yunusov, KhPS [Chemistry of Natural Compounds], 5, 455, 1969.
2. Judith A. Bosson, M. Rasmussen, E. Ritchie, A. V. Robertson, and W. C. Taylor, Austral. J. Chem., 16, 480, 1963.
3. R. Aneja, S. K. Mukerjee, and T. R. Seshadri, Tetrah., 4, 256, 1958.
4. S. M. Sharafutdinova and S. Yu. Yunusov, KhPS [Chemistry of Natural Compounds], 4, 198, 164, 1968.
5. Organic reactions [Russian translation], collection 2, Moscow, 7, 1950.
6. B. D. Paul and P. K. Bose, J. Indian Chem. Soc., 45, 552, 1968.

2 July 1969

Institute of the Chemistry of Plant Substances AS UzSSR